

### **REMARKS**

Applicants respectfully request entry of the Amendment and reconsideration of the claims. Please cancel claims 1-5, 19-20, and 26-28 without prejudice. Applicants have amended claims 8-14, 16-18, 21-25, and 29-30, and added new claim 31. Support can be found throughout the specification. Claims 6-18, 21-25, and 29-31 will be pending upon entry of this amendment.

#### **Amendments to the Claims**

Claims 9 and 10 have been amended to link to the composition claim of claim 6.

Claims 8, 11, and 29-30 have been amended to change the transition term from "including" to "comprising".

Claims 12 and 14 have been amended to establish the abbreviations without quotation marks.

Claims 16-18 and 21-25 have been amended to change the dependency of these claims from claim 1 to claim 9.

Claim 13 has been amended to change the dependency from claim 12 to claim 9.

#### **Response to the Restriction Requirement**

The Examiner has required restriction of the claims of the above-noted application to one of the following inventions under 35 U.S.C § 121:

- I. Claims 1-5 and 16-28, drawn to manufacture of a medicament using a nitric oxide increasing compound and a glutathione increasing compound useful in the treatment of insulin resistance.
- II. Claims 6-8, 11, 29 and 30, drawn to a pharmaceutical composition comprising a hepatic nitric oxide increasing compound and a glutathione increasing compound.
- III. Claims 9, 10, 12-15 and 26-28, drawn to a method of reducing insulin resistance having a lower than normal hepatic glutathione levels in a mammalian patient.

The Examiner has further required election of species for the glutathione increasing compound and the nitric oxide increasing compound in claims 4, 5, 7, 14, 15, 27, and 28.

Without acquiescing to the statements made in the Restriction Requirement, Applicants hereby elect with traverse the claims of Group II (claims 6-8, 11, 29, and 30 (the pharmaceutical composition claims)) for prosecution in the instant application.

Without acquiescing to the statements made in the Restriction Requirement, Applicants hereby elect with traverse the species of N-acetylcysteine as the glutathione-increasing compound, and elect with traverse the species of SIN-1 as the nitric oxide-increasing compound.

**Traversal.** Since this application is a national stage entry under 35 U.S.C. § 371 and as the Examiner notes, restriction of claims is to comply with the Unity of Invention standard under PCT Rules 13.1 and 13.2.

PCT Rule 13.1 states that "[t]he international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. MPEP § 1850. Further, PCT Rule 13.2 recites

[w]here a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

Under MPEP § 1850(III)(A) the combination of an independent claim for a product and an independent claim for a use of said product constitutes one invention and does not merit restriction under PCT Rule 13 for Unity of Invention.

The method for determining unity of invention under PCT Rule 13 shall be construed as permitting, in particular, the inclusion of any one of the following combinations of claims of different categories in the same international application: (A) In addition to an independent claim for a given product, an independent claim for a process specially adapted for the manufacture of the said product, and an independent claim for a use of said product; or...

Therefore, a product claim and a method of using said product do not constitute separable inventions. Applicants respectfully assert that the instant Group II and Group III claims should be examined in the same application.

The Examiner asserts that Groups I to III lack unity because they lack the same or corresponding special technical features. The Examiner states that Stoyanovsky et al. (*Cell Calcium*, 1997, 21(1), 19-29) disclose cysteine (glutathione-increasing compound) and nitrosylated cysteine (nitric oxide increasing compound) in a buffer medium at physiological pH of 7.0 (page 25-26, bridging paragraph in column 2). Thus, the Examiner alleges that the technical feature of the instant claims is not a contribution over the cited art.

Applicants respectfully submit that Stoyanovsky et al. do not disclose both cysteine and nitrosylated cysteine in a physiologic buffer. At lines 9 to 10 of the cited paragraph, Stoyanovsky et al. disclose a medium at physiological pH of 7.0 with 50  $\mu$ M cysteine. There is no disclosure of nitrosylated cysteine in the same physiologic buffer with the cysteine. Rather, the sentence bridging p. 25-26 recites

the potentiation of NO gas by cysteine in the presence of oxygen *is consistent* with the *predicted interaction* of NO and O<sub>2</sub> *resulting in the formation of N<sub>2</sub>O<sub>3</sub>* which readily nitrosylates low molecular weight thiols like cysteine and glutathione to produce R-SNO compounds [11]. [*emphasis added*]

Thus, Stoyanovsky et al. do not disclose both cysteine and nitrosylated cysteine in a physiologic buffer. As such, Applicants respectfully assert that the Examiner has not demonstrated the technical feature in the prior art. Thereby, Applicants respectfully request Group II and Group III claims be rejoined as having the same technical feature.

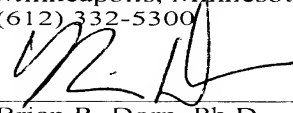
#### **Request for Rejoinder**

Following the Amendment, method claims 9-10, 12-18, 21-25, and 31 are linked to the elected pharmaceutical composition claim 6. If the Examiner does not withdraw the instant restriction requirement, Applicants hereby request rejoinder of non-elected claims 9-10, 12-18, 21-25, and 31 under MPEP § 821.04(b) upon the allowability of claim 6.

If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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